European Review for Medical and Pharmacological Sciences 2023; 27: 1824-1830

A novel marker to predict cardiac arrhythmia in epilepsy patients: frontal QRS-T angle

U. DUZGUN[1], M.B. TASCANOV[2], J. SHAFIYEV[3], M. OCAK[4], I.H. YASAK[5], H. FEDAI[2], K. TOPRAK[2], B. GUNGORER[6], U.B. SIMSEK[1], O. KARADAS[3]

[1]Department of Neurology, University of Health Sciences, Gulhane Training and Research Hospital, Ankara, Turkey
[2]Department of Cardiology, Faculty of Medicine, Harran University, Sanliurfa, Turkey
[3]Department of Neurology, Gülhane Faculty of Medicine, University of Health Sciences, Ankara, Turkey
[4]Gazi State Hospital, Emergency Clinic, Samsun, Turkey
[5]Department of Emergency Medicine, Faculty of Medicine, Harran University, Sanliurfa, Turkey,
[6]Department of Emergency Medicine, University of Health Sciences, Ankara Etlik City Hospital, Ankara, Turkey

Abstract. – OBJECTIVE: The most important complication of epilepsy, which is a chronic disorder of the central nervous system, is sudden unexplained death in epilepsy (SUDEP). The causes of SUDEP are complex and multifactorial. Epilepsy patients are at increased risk of cardiovascular events, SUDEP, and ventricular arrhythmias, due to both the disease itself and the effect of antiseizure medications. Previous studies have commonly focused on cardiac repolarization markers in epilepsy patients. This study aimed to investigate frontal QRS-T angle (FTQ angle), a relatively new repolarization parameter, in epilepsy patients.

PATIENTS AND METHODS: One hundred two epilepsy patients and 86 healthy volunteers as a control group were included in the study. The clinical data of all patients were prospectively recorded during patient visits. All participants underwent 12-lead surface electrocardiography (ECG). SPSS 22 was used to evaluate all data. $p<0.05$ was considered statistically significant.

RESULTS: When the epilepsy patient group and the control group were compared in terms of QRS (89.59±43.63 *vs.* 80.00±9.82, $p=0.050$), QT (364.30±36.16 *vs.* 335.95±35.64, $p<0.001$), QTc (418.85±27.06 *vs.* 409.37±26.66, $p=0.018$) durations, and FTQ angle (46.55±22.06 *vs.* 20.84±12.70, $p<0.001$), statistically significant differences were found between the groups. We observed that FTQ angle was significantly higher in individuals exposed to the disease for more than 10 years (39.2±19.0 *vs.* 54.7±22.5, $p<0.001$). In addition, according to the multivariate logistic regression analysis, disease duration was an independent predictor of FTQ angle (β=0.263, $p=0.009$).

CONCLUSIONS: FTQ angle, a relatively new repolarization parameter, can be used as an inexpensive, easy, reproducible, and reliable ECG marker to predict the risk of adverse cardiac events in epilepsy patients.

Key Words:
Epilepsy, Frontal QRS-T angle, Cardiac arrhythmia, Sudden unexpected death, Antiseizure medications.

Introduction

Epilepsy is a chronic disorder of the central nervous system characterized by recurrent seizures, unusual behaviors, and loss of consciousness due to abnormal electrical activity in the brain[1,2]. Sudden unexpected death in epilepsy (SUDEP) is the most serious complication of this condition. Patients with epilepsy have a higher risk for sudden unexpected death than nontraumatic individuals without epilepsy[3]. SUDEP is usually independent of status epilepticus (SE) and is associated with generalized tonic-clonic seizures[4]. The causes of SUDEP are complex and multifactorial. Many factors, including autonomic dysfunction, cardiac arrhythmia, antiseizure medications (ASMs), and heart rate variability, are thought[5] to be responsible for the development of SUDEP.

The relation between seizures and arrhythmia is complex and is thought to involve the presence of conductive cardiac and neuronal tissue, cardiac and neural action potentials, and Na^+ and K^+ channels both in the heart and in the brain. Histologically, the cardiac conduction system is similar to highly specialized nerve cells, so the conduction and excitability of cardiac and neuronal cells show similar properties[6]. Hence, cardiac

Corresponding Author: Ülkühan Düzgün, MD; e-mail: ulkuhanduzgun@hotmail.com

autonomic dysfunction, heart rate irregularity, ventricular arrhythmia, and SUDEP occur at high rates in patients with epilepsy[7].

Previous studies[8-10] have shown that ASMs increase the risk for cardiovascular events, such as stroke, myocardial infarction, and arrhythmia. Therefore, epilepsy patients have increased risks of cardiovascular events, SUDEP, and ventricular arrhythmia due to both the disease itself and the effect of ASMs. Electrocardiogram (ECG) changes in the ictal, interictal, and postictal periods have been investigated in epilepsy patients. Such studies[1,8,11,12] have focused on cardiac repolarization markers and have concluded that epilepsy patients show prolonged or short QT, increased QT dispersion (QTd), increased corrected QT dispersion (QTcd), and heart rate abnormalities. In addition, patients receiving ASMs show ECG abnormalities, such as increased atrioventricular block, bradycardia, arrhythmia, increased QT and QTc durations, and increased QTd and QTcd[1,13,14].

Frontal QRS-T angle (FQT angle) is a relatively new indicator of ventricular repolarization heterogeneity, which is an indicator of ventricular arrhythmia[15,16]. To the best of our knowledge, there have been no previous reports regarding FQT angle in epilepsy patients. The present study investigated FQT angle in patients with epilepsy and to determine its relationship with the duration of epilepsy.

Patients and Methods

Study Population

In this prospective study, 102 epilepsy patients aged 18 years and older who were followed-up in the epilepsy outpatient clinic of a tertiary health institution were included. Patients under 18 years of age or with hypertension, known coronary artery disease, heart failure, moderate or severe valve disease, or a history of arrhythmia were excluded from the study. The control group consisted of 86 healthy volunteers of similar age and sex without heart or neurological disease.

Informed consent was obtained from all participants of the study. Necessary permission for the study procedures was obtained from the Harran University Faculty of Medicine Ethics Committee. The study was conducted in accordance with the revised Declaration of Helsinki criteria.

Study Procedure

The demographic characteristics of all participants and the patients' birth history, family history of epilepsy, history of febrile convulsions, epileptic seizure type, epileptic seizure onset time, disease duration, frequency of epileptic seizures, history of status epilepticus (SE), presence of cranial magnetic resonance (MR) findings, electroencephalography (EEG) findings, information about ASM taken, and presence of drug-resistant epilepsy were recorded during the patients' visits. A 12-lead baseline ECG (model ECG-1350K Nihon-Kohden Corporation, Tokyo, Japan) with a height of 10 mm/mV and a velocity of 25 mm/s was obtained from all participants both in the supine position and at rest. Figure 1 shows how the FQT angle was measured.

The 2017 International League Against Epilepsy (ILEA) classification was used in the classification of epileptic seizures[17]. Seizure frequency was classified as follows: daily, every week, every month, less than once a month, once a year or less, and absence of seizures for more than 2 years. Failure to achieve sustained seizure remission, despite taking appropriately selected 2 or more tolerable therapeutic doses of ASMs, was accepted as resistant epilepsy[18].

The EEG findings of the patients were evaluated according to the ILEA criteria. Patients with no abnormality in their interictal EEG were classified as normal. Interictal epileptic discharge (IED) was defined as the presence of sharp, spike, and multiple spike waves in those with interictal EEG abnormalities. To better understand the effect of epilepsy duration on FQT angle, the epilepsy patients were divided into two groups: those exposed to the disease for ≥10 years (group I, n=50) and those exposed for <10 years (group II, n=52).

Statistical Analysis

SPSS 22 (IBM Corp., Armonk, NY, USA) was used to evaluate all data. The Kolmogorov-Smirnov test was used to evaluate whether the data fit the normal distribution. Student's *t*-test was used for parameters that were normally distributed, while the Mann-Whitney U test was used for parameters that were not normally distributed. Correlations were tested using Spearman's analysis. Categorical variables were compared using the Chi-square test. Continuous variables were presented as mean ± standard deviation or median (interquartile range), while categorical variables were presented as percentages. Multivariate regression analysis was performed to determine independent predictors of FQT angle. $p<0.05$ was considered statistically significant.

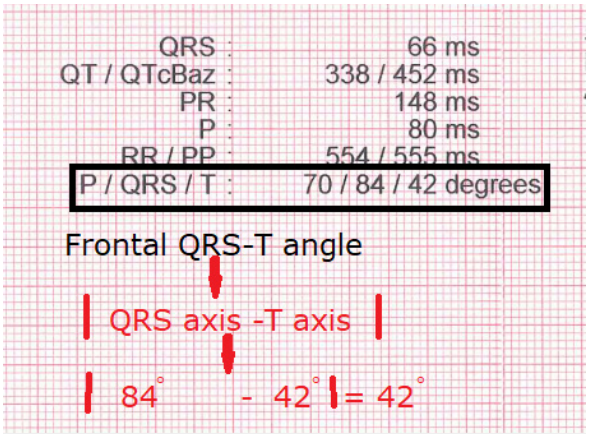

Figure 1. Model for measuring the FTQ Angle.

Results

In total, 102 epilepsy patients and 86 healthy volunteers as controls were included in this study. The clinical and demographic characteristics of the study population are shown in Table I. The clinical features of the epilepsy patients are shown in Table II. There were no statistically significant differences in demographic characteristics, including age and sex, between the two groups. However, there were significant differences between the control and epilepsy patient groups in QRS (89.59±43.63 *vs.* 80.00±9.82, p=0.050), QT (364.30±36.16 *vs.* 335.95±35.64, p<0.001), QTc interval (418.85±27.06 *vs.* 409.37±26.66, p=0.018) and FQT angle (46.55±22.06 *vs.* 20.84±12.70, p<0.001) (Table I).

To better understand the effect of disease duration on FQT angle, we divided the epilepsy group into two groups according to disease duration: <10 years (n = 52) and ≥10 years. FQT angle was significantly higher in individuals with disease duration ≥ 10 years than <10 years (respectively, 39.2±19.0 *vs.* 54.7±22.5 p<0.001), In addition, correlation analysis revealed a positive correlation between FQT angle and disease duration (r=0.302, p=0.002). Moreover, in multivariate regression analysis, disease duration was an independent predictor of FQT angle (β=0.263, p=0.009) (Table III). In addition, FQT angle was significantly higher in patients with than without a history of SE and IED on EEG (Table IV).

Discussion

FQT angle, a relatively new repolarization parameter, was investigated in epilepsy patients. The angle was significantly higher in epilepsy patients than in healthy controls. Moreover, disease duration was an independent predictor of FQT angle in epilepsy patients. In addition, the angle was higher in patients with than without a history of SE and IED.

Previous studies[1,7,8,11,12,19] have investigated a number of repolarization markers in epilepsy patients, and showed that QT, QTc, and QRS are significantly higher in patients with epilepsy compared to healthy controls. In addition, patients receiving ASMs show ECG abnormalities, such as increased atrioventricular block, increased QT and QTc, and increased QTd and QTcd[1,13].

QT interval is an indicator of the ventricular depolarization and repolarization period. QTc interval and QTcd are cardiac repolarization abnormalities associated with sudden cardiac death and ventricular tachyarrhythmia[20]. The observation that these values were higher in epilepsy patients suggests that these parameters may be related to the increased risk for ventricular arrhythmia and SUDEP in these patients. Consistent with the literature, QRS duration, QT, and QTc were higher in the epilepsy patients than controls in the present study. The pathogenesis of increased

Table I. Comparison of the demographic and clinical characteristics of the participants.

Parameters	Epilepsy Group (n=102)	Control Group (n=86)	*p*-values
Male, %	43 (42.2)	35 (40.7)	0.946*
Age (years)	36.08±14.43	36.25±11.27	0.929
Heart rate (per/min)	81.29±13.96	80.99±12.53	0.876
QT (ms)	364.30±36.16	335.95±35.64	<0.001
QTc (ms)	418.85±27.06	409.37±26.66	0.018
FTQ angle (°)	46.55±22.06	20.84±12.70	<0.001
QRS time (ms)	89.59±43.63	80.00±9.82	0.050

*Chi-square test; Independent samples test. FTQ angle: frontal QRS-T angle.

Table II. Clinical characteristics of the epilepsy patients.

Disease Duration, Years		
Mean+SD		12.22 ±10.85
Difficult birth history (%)	Yes	12 (14.8%)
	No	69 (85.2%)
Febrile convulsion history (%)	Yes	20 (25.0%)
	No	60 (75.0%)
Family history of epilepsy (%)	Yes	12 (15.6%)
	No	65 (84.4%)
Abnormal finding on MRI (%)	Yes	22 (28.6%)
	No	55 (71.4%)
History of status epilepticus (%)	Yes	10 (9.8%)
	No	92 (90.2%)
Interictal EEG abnormality (%)	Yes	75 (79.8%)
	No	19 (20.2%)
IED (%)	Yes	25 (26.6%)
	No	69 (73.4%)
Use of ASMs (%)	Monotherapy	65 (63.7%)
	Polytherapy	37 (36.3%)
Presence of resistant epilepsy (%)	Yes	1 (13.0%)
	No	87 (87.0%)
Seizure type		
Focal onset (%)		64 (62.7%)
Focal (%)		21 (20.6%)
Awareness (%)		2 (2.0%)
Impaired awareness (%)		19 (18.6%)
Focal to bilateral tonic-clonic (%)		43 (42.2%)
Generalized onset (%)		28 (27.5%)
Motor (%)		27 (26.5%)
Motor/Myoclonic (%)		3 (2.9%)
Motor/Myoclonic+Tonic-Clonic (%)		13 (12.7%)
Motor/Tonic-Clonic (%)		11 (10.8%)
Non-Motor (%)		1 (1.0%)
Unknown onset (%)		10 (9.8%)
Tonic-Clonic (%)		8 (7.8%)
Unclassified (%)		2 (2.0%)
Seizure frequency		
Every day (%)		5 (4.9%)
Every week (%)		11 (10.8%)
Every month (%)		19 (18.6%)
Less than once a month (%)		17 (16.7%)
Once a year or less (%)		27 (26.5%)
No seizures for more than 2 years (%)		23 (22.5%)

SD: Standard Deviation, MRI: Magnetic Resonance Imaging, EEG: Electroencephalography, ASMs: Antiseizure medications, IED: Interictal Epileptic Discharge.

cardiac electrophysiological abnormalities seen in patients with epilepsy is complex. A number of mechanisms, including cardiac autonomic dysfunction, heart rate variability, microstructural changes in the heart due to seizures, cardiac damage due to ictal hypoxemia, cardiac damage due to catecholamine discharge released during seizures, neuronal and cardiac ion channel dysfunction, and multiple gene mutations associated with arrhythmia, have been suggested[7,21-24] to be associated with increased cardiac events and arrhythmia risk in patients with epilepsy.

Most patients with epilepsy are taking ASMs, which have an indirect protective effect by reducing the frequency of seizures. However, these agents may also have cardiotoxic effects[25].

Table III. Multiple Linear Regression Analysis for Predictors of FTQ Angle.

	Unstandardized coefficients		Standardized coefficients		
	B	SE*	β	*t*	*p*
Age	0.012	0.151	0.008	0.083	0.934
SE History	12.368	7.126	0.169	1.736	0.086
Seizure Frequency	0.438	1.401	0.030	0.313	0.755
IED	7.415	4.382	0.160	1.692	0.094
Disease Duration	0.534	0.199	0.263	2.678	0.009

SE*: Standard Error, B: Unstandardized Regression Coefficient, β: Standardized β Coefficient, SE: Status Epilepticus, IED: Interictal Epileptic Discharge, FTQ Angle: Frontal QRS-T Angle.

The metabolic effects of some ASMs, including hyperlipidemia, increased production of proinflammatory molecules, weight gain, and metabolic syndrome, may increase the risk for cardiovascular events[25-28]. ASMs that primarily block sodium channels may affect cardiac sodium channels and cause sudden cardiac death[25,29]. These cardiac side effects of both epilepsy and ASMs have prompted research regarding this issue. In the present study, we found no significant differences in cardiac side effects between patients treated with monotherapy and polytherapy.

Progress in cardiology has brought an increased understanding of the effects of ECG in detecting cardiac diseases and predicting risk before the development of cardiac disease[16,30]. Myocardial repolarization has traditionally been evaluated according to the QT interval. As this range is heart rate-dependent, it is usually measured and reported as the QTc. Investigations[1,7,8,11,14] of ECG changes in epilepsy patients generally focus on ventricular repolarization markers, such as QT/Qtd/Qtc/Qtcd. Calculation of QT and QTc is difficult and requires additional tools, including a magnifying glass and/or computer programs. In addition, the repeatability of these parameters is poor and is affected by heart rate. Therefore, there has been a move toward new parameters that can be measured easily from ECG[15,16,31]. The FQT angle, defined as the angle between the QRS wave showing ventricular depolarization and the T wave showing ventricular repolarization, is a new marker of ventricular repolarization heterogeneity. It can easily be measured by subtracting the T wave value from the QRS wave value from the surface ECG. In addition, 12-lead ECG devices usually calculate the QRS and T wave values automatically[31]. Previous studies[31-33] have shown that FQT angle is a more powerful and reproducible marker of ventricular repolarization that is less affected by external factors than QT. In the present study, FQT angle was significantly higher in the epilepsy group than the control group. Moreover, we found that the duration of the epilepsy was an independent predictor of FQT angle. In addition, FQT angle was significantly higher in patients with a history of SE and IED on EEG, which are among the negative clinical pictures of epilepsy, compared to epileptic patients without these clinical features.

Table IV. Comparison of FTQ angle according to the clinical manifestations of the epilepsy patients.

		FTQ Angle	*p*-values
SE History			
No	92	44.66±22.18	0.008
Yes	10	63.90±10.62	
IED			
No	68	42.26±22.81	0.005
Yes	34	55.12±17.87	

SE: Status Epilepticus, IED: Interictal Epileptic Discharge, FTQ Angle: Frontal QRS-T Angle.

Limitations

The main limitations of our study were the relatively small number of patients, the fact that the FQT angle could not be compared in terms of the ASMs used by the patients, and the lack of arrhythmia monitoring of the patients (with 24 h continuous ECG monitoring or Holter ECG monitoring). Further studies addressing these limitations are required to confirm our findings.

Conclusions

Prolonged epilepsy is an independent predictor of FQT angle, a reproducible and reliable repolariza-

tion parameter, which can be used to predict the risk for cardiac arrhythmia in patients with epilepsy.

Conflict of Interest
The Authors declare that they have no conflict of interests.

Funding
No funding supported this research.

Authors' Contributions
Concept: U. Duzgun, M. B. Tascanov, I. H. Yasak; Design: U. Duzgun, M. B. Tascanov, I. H. Yasak, M. Ocak; Supervision: U. Duzgun, M. B. Tascanov, U. B. Sımsek, O. Karadas; Materials: U. Duzgun, K. Toprak, H. Fedai, J. Shafiyev, U. B. Sımsek, B. Gungorer; Data collection and/or processing: U. Duzgun, K. Toprak, H. Fedai, B. Gungorer, J. Shafiyev; Analysis and/or interpretation: U. Duzgun, M. B. Tascanov, M. Ocak; Literature search: I. H. Yasak, H. Fedai, J. Shafiyev, B. Gungorer; Writing: U. Duzgun, M. B. Tascanov, I. H. Yasak, M. Ocak, K. Toprak; Critical review: U. B. Sımsek, O. Karadas. All authors have read and agreed to the published version of the manuscript.

Ethics Approval
This study was approved by the Harran University Faculty of Medicine Ethics Committee (date: 07/02/2022, No. 22/03/06).

Informed Consent
Informed consent was obtained from all the participants of the study.

ORCID ID
Ülkühan Düzgün: 0000-0001-9759-6960.
Mustafa Begenc Tascanov: 0000-0002-9008-6631.
Javid Shafiyev: 0000-0002-3334-979X.
Metin Ocak: 0000-0002-9978-0216.
İbrahim Halil Yasak: 0000-0002-6399-7755.
Halil Fedai: 0000-0003-2087-0989.
Kenan Toprak: 0000-0001-8923-8709.
Bülent Güngörer: 0000-0002-9856-7181.
Uğur Burak Şimşek: 0000-0003-4688-7658.
Ömer Karadaş: 0000-0003-0457-3722.

References

1) Asoğlu R, Özdemir M, Aladağ N, Asoğlu E. Evaluation of Cardiac Repolarization Indices in Epilepsy Patients Treated with Carbamazepine and Valproic Acid. Medicina (Kaunas) 2020; 56: 20.
2) Ghosh S, Sinha JK, Khan T, Devaraju KS, Singh P, Vaibhav K, Gaur P. Pharmacological and Therapeutic Approaches in the Treatment of Epilepsy. Biomedicines 2021; 9: 470.
3) Ficker DM, So EL, Shen WK, Annegers JF, O'Brien PC, Cascino GD, Belau PG. Population-based study of the incidence of sudden unexplained death in epilepsy. Neurology 1998; 51: 1270-1274.
4) Surges R, Sander JW. Sudden unexpected death in epilepsy: mechanisms, prevalence, and prevention. Curr Opin Neurol 2012; 25: 201-207.
5) Costagliola G, Orsini A, Coll M, Brugada R, Parisi P, Striano P. The brain-heart interaction in epilepsy: implications for diagnosis, therapy, and SUDEP prevention. Ann Clin Transl Neurol 2021; 8: 1557-1568.
6) Borowicz KK, Banach M. Antiarrhythmic drugs and epilepsy. Pharmacol Rep 2014; 66: 545-551.
7) Suna N, Suna I, Gutmane E, Kande L, Karelis G, Viksna L, Folkmanis V. Electrocardiographic Abnormalities and Mortality in Epilepsy Patients. Medicina (Kaunas) 2021; 57: 504.
8) Lee-Lane E, Torabi F, Lacey A, Fonferko-Shadrach B, Harris D, Akbari A, Lyons RA, Rees MI, Sawhney I, Halcox J, Powell R, Pickrell WO. Epilepsy, antiepileptic drugs, and the risk of major cardiovascular events. Epilepsia 2021; 62: 1604-1616.
9) Chang CS, Liao CH, Lin CC, Lane HY, Sung FC, Kao CH. Patients with epilepsy are at an increased risk of subsequent stroke: a population-based cohort study. Seizure 2014; 23: 377-381
10) Olesen JB, Abildstrøm SZ, Erdal J, Gislason GH, Weeke P, Andersson C, Torp-Pedersen C, Hansen PR. Effects of epilepsy and selected antiepileptic drugs on risk of myocardial infarction, stroke, and death in patients with or without previous stroke: a nationwide cohort study. Pharmacoepidemiol Drug Saf 2011; 20: 964-971.
11) Drake ME, Reider CR, Kay A. Electrocardiography in epilepsy patients without cardiac symptoms. Seizure 1993; 2: 63-65.
12) Teh HS, Tan HJ, Loo CY, Raymond AA. Short QTc in epilepsy patients without cardiac symptoms. Med J Malaysia 2007; 62: 104-108.
13) Aslan K, Deniz A, Demir T, Karaaslan B, Bozdemir H. Is cardiac repolarization time different between epilepsy patients on antiepileptic drugs and healthy subjects? J. Turk. Chapter ILAE 2018; 24: 15-20.
14) Lanza GA, Coll M, Grassi S, Arena V, Campuzano O, Calò L, De Ruvo E, Brugada R, Oliva A. An enigmatic case of cardiac death in an 18-years old girl. Eur Rev Med Pharmacol Sci 2021; 25: 4999-5005.
15) Tascanov MB, Tanriverdi Z, Gungoren F, Besli F, Bicer Yesilay A, Altiparmak HI, Bayram G, Demir K. The effect of propofol on frontal QRS-T angle in patients undergoing elective colonoscopy procedure. J Clin Pharm Ther 2020; 45: 185-190.
16) Ocak M, Tascanov MB, Yurt NŞ, Yurt YC. A new predictor for indicating clinical severity and prognosis in COVID-19 patients: Frontal QRS-T angle. Am J Emerg Med 2021; 50: 631-635.
17) Scheffer IE, Berkovic S, Capovilla G, Connolly MB, French J, Guilhoto L, Hirsch E, Jain S, Mathern GW, Moshé SL, Nordli DR, Perucca E, Tomson T, Wiebe S, Zhang YH, Zuberi SM. ILAE classifica-

tion of the epilepsies: Position paper of the ILAE Commission for Classification and Terminology. Epilepsia 2017; 58: 512-521.

18) Kwan P, Arzimanoglou A, Berg AT, Brodie MJ, Allen Hauser W, Mathern G, Moshé SL, Perucca E, Wiebe S, French J. Definition of drug resistant epilepsy: consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies. Epilepsia 2010; 51: 1069-1077.
19) Dogan EA, Dogan U, Yildiz GU, Akilli H, Genc E, Genc BO, Gok H. Evaluation of cardiac repolarization indices in well-controlled partial epilepsy: 12-Lead ECG findings. Epilepsy Res 2010; 90: 157-163.
20) Morita H, Wu J, Zipes DP. The QT syndromes: long and short. Lancet 2008; 372: 750-763.
21) P-Codrea Tigaran S, Dalager-Pedersen S, Baandrup U, Dam M, Vesterby-Charles A. Sudden unexpected death in epilepsy: is death by seizures a cardiac disease? Am J Forensic Med Pathol 2005; 26: 99-105.
22) Moseley BD, Wirrell EC, Nickels K, Johnson JN, Ackerman MJ, Britton J. Electrocardiographic and oximetric changes during partial complex and generalized seizures. Epilepsy Res 2011; 95: 237-245.
23) Lerche H, Shah M, Beck H, Noebels J, Johnston D, Vincent A. Ion channels in genetic and acquired forms of epilepsy. J Physiol 2013; 591: 753-764.
24) Goldman AM, Glasscock E, Yoo J, Chen TT, Klassen TL, Noebels JL. Arrhythmia in heart and brain: KCNQ1 mutations link epilepsy and sudden unexplained death. Sci Transl Med 2009; 1: 2-6.
25) Zaccara G, Lattanzi S, Brigo F. Cardiac adverse effects of antiseizure medications. Expert Opin Drug Saf 2022; 21: 641-652.
26) Yamamoto Y, Terada K, Takahashi Y, Imai K, Kagawa Y, Inoue Y. Influence of antiepileptic drugs on serum lipid levels in adult epilepsy patients. Epilepsy Res 2016; 127: 101-106.
27) Elliott JO, Jacobson MP, Haneef Z. Cardiovascular risk factors and homocysteine in epilepsy. Epilepsy Res 2007; 76: 113-123.
28) Verrotti A, Manco R, Agostinelli S, Coppola G, Chiarelli F. The metabolic syndrome in overweight epileptic patients treated with valproic acid. Epilepsia 2010; 51: 268-273.
29) Maadarani O, Bitar Z, Ashkanani A, Elzoueiry M, Elhabibi M, Gohar M, Almuwaizri M, Shoeb S, Alsaddah J. Cardiac Sodium Channel Blockade Due to Antiepileptic Drug Combination. Eur J Case Rep Intern Med 2021; 8: 002839.
30) Topaloğlu O, Çimci M. The frontal QRS-T angle in patients with incidentally discovered nonfunctional adrenal adenomas. Eur Rev Med Pharmacol Sci 2021; 25: 3028-3037.
31) Colluoglu T, Tanriverdi Z, Unal B, Ozcan EE, Dursun H, Kaya D. The role of baseline and post-procedural frontal plane QRS-T angles for cardiac risk assessment in patients with acute STEMI. Ann Noninvasive Electrocardiol 2018; 23: e12558.
32) Gotsman I, Keren A, Hellman Y, Banker J, Lotan C, Zwas DR. Usefulness of electrocardiographic frontal QRS-T angle to predict increased morbidity and mortality in patients with chronic heart failure. Am J Cardiol 2013; 111: 1452-1459.
33) Kuyumcu MS, Ozen Y, Ozbay MB. COVID-19 survivors may exhibit deterioration in frontal plane QRS-T angle and other electrocardiogram parameters. Eur Rev Med Pharmacol Sci 2022; 26: 6879-6884.